

Claims

I claim:

- 5 1. A method of transporting an pharmacologically active form of Substance P, or neuropeptide, across the blood-brain barrier into the central nervous system of a living subject using the chimeric hybrid molecule comprising a cyclic alkaloid moiety which binds as an agonist to a mammalian or human mu (μ) opioid receptor and a
10 peptide moiety which binds as an agonist to a mammalian/human substance P.
2. A method of transporting a pharmacologically active form of substance P, or neuropeptide, across the blood-brain barrier into
15 the central nervous system of a living subject using the active metabolite of morphine, morphine 6-glucuronide, contained within chimeric hybrid molecules wherein:
 - a. One moiety of the chimeric hybrid molecule binds as an
20 agonist to the mu (μ) opioid receptor and the other moiety of which binds as an agonist to the substance P receptor comprised of:

(i) chemically modified morphine in which morphine covalently linked through its 6'OH group comprises the mu (μ) opioid receptor agonist moiety;

5 (ii) the substance P fragment N-acetyl-SP [3-11]:
sequence of Ac-KPQQFFGLM-NH₂ (SEQ. ID. NO. 1),
covalently linked through its ϵ (epsilon) amino
group, which comprises the substance P receptor
agonist moiety; and

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(iii) the six carbon carbohydrate d-glucuronic acid,
covalently cross linking morphine through its 6'OH
group via an o-glycosidic bond to the ϵ (epsilon)
amino group of the substance P fragment N-acetyl-SP
15 [3-11] via a pseudo peptide bond, which comprises a
compact molecular hinge linking the two moieties;
or

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b. One moiety of the chimeric hybrid molecule binds as an
20 agonist to the mu (μ) opioid receptor and the other
moiety of which binds as an agonist to the substance P
receptor comprised of:

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(i) chemically modified morphine in which morphine covalently linked through its 6'OH group comprises the mu (μ) opioid receptor agonist moiety;

5 (ii) the substance P fragment SP [5-11]: sequence of QQFFGLM-NH₂ (SEQ. ID. NO. 2), covalently linked through its α (alpha) amino group, which comprises the substance P receptor agonist moiety; and

10 (iii) the six carbon carbohydrate d-glucuronic acid, covalently cross linking morphine through its 6'OH group via an o-glycosidic bond to the α (alpha) amino group of the substance P fragment SP [5-11] via a pseudo peptide bond, which comprises a
15 compact molecular hinge linking the two moieties,
or

c. A chimeric hybrid molecule one moiety of which binds as an agonist to the mu (μ) opioid receptor and the other
20 moiety of which binds as an agonist to the substance P receptor comprised of:

(i) chemically modified morphine in which morphine covalently linked through its 6'OH group comprises the mu (μ) opioid receptor agonist moiety;

5 (ii) the substance P fragment SP [7-11]: sequence of FFGLM-NH₂ (SEQ. ID. NO. 3), covalently linked through its α (alpha) amino group, which comprises the substance P receptor agonist moiety; and

10 (iii) the six carbon carbohydrate d-glucuronic acid, covalently cross linking morphine through its 6'OH group via an o-glycosidic bond to the α (alpha) amino group of the substance P fragment SP [7-11] via a pseudo peptide bond, which comprises a
15 compact molecular hinge linking the two moieties.